Third Quarterly Progress Report

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Feasibility of an Intra-neural Auditory Prosthesis Stimulating Electrode Array

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1. Introduction

The objective of this research is to evaluate the feasibility of intra-neural stimulation as a means of auditory prosthesis. We are stimulating the auditory nerve with penetrating multi-channel electrode arrays and monitoring the tonotopic spread of activation in the central nucleus of the inferior colliculus (ICC) of cats. In the present quarter, we continued our studies using 16-site single-shank silicon-substrate stimulating electrode arrays (i.e., “Michigan” electrodes) inserted into the auditory nerve via a lateral trans-bulla approach. We extended our previous studies of tonotopic activation, began tests of temporal integration, and completed measures of interactions between simultaneously stimulated electrodes. We presented some preliminary results as a poster at the Neural Interface Workshop in Bethesda (September 7-9, 2006).

2. Summary of activities for the quarter

We conducted acute physiological experiments in four cats, using acoustic stimulation and electric stimulation via intra-scalar and intra-neural electrodes. Responses were recorded using 32-channel recoding probes inserted into the contralateral ICC and fixed in place. Each animal was tested first in normal-hearing conditions using acoustic stimulation consisting of tones, noise bursts, and varying-rate click trains. Next, the ear was deafened with an intra-scalar injection of neomycin and an 8-electrode intra-scalar, banded-array electrode was implanted in the scala tympani. These arrays were stimulated with single biphasic electrical pulses and trains of such pulses. Finally, the intra-scalar electrode was removed and a 16-site stimulating array was inserted into the auditory nerve through a small hole in the osseous wall of the modiolus.

Responses to acoustic and intra-scalar stimulation were obtained in all four cats. Intra-neural stimulation was fully successful, however, in only two of the cats because of the difficulty of passing a fragile and highly flexible silicon-substrate stimulating array past bony structures into the nerve. In one of the four cats studied this quarter, we never achieved satisfactory insertion of an electrode into the nerve. In a second animal, insertion was achieved after some difficulty, but we found unusually high thresholds for stimulation of middle- and apical- turn fibers and no response to stimulation of basal-turn fibers. Our interpretation in that case was that we had somehow damaged the nerve. In the remaining two cats, we observed low thresholds for intra-neural stimulation and access to fibers from base through apex, consistent with our observations reported in previous quarterly progress reports. Physiological results discussed below were obtained from those two animals. Detailed *post-mortem* dissections were performed on all four cats to aid in our understanding of the anatomical relationships of nerve branches and surrounding bone.

In the animals that were successfully implanted with an intra-neural electrode, we began tests of temporal integration of electrical pulses, comparing intra-scalar and intra-neural stimulation. Previous studies have stimulated the auditory nerve with pairs of pulses varying in inter-pulse interval. Current levels were varied to determine the threshold for stimulation of individual auditory nerve fibers. Those threshold measurements could be fit with an exponential function, yielding a time constant. In these previous cat studies, intra-meatal stimulation (Cartee et al., 2000) yielded a time constant of ~150 µs, whereas the time constant for intra-scalar stimulation was substantially longer: 504 µs (estimated by Cartee et al. from data in Dynes, 1996). In a study in guinea pigs using intra-scalar stimulation with recording from the auditory cortex, we obtained a time constant comparable to the previous intra-scalar value: ~350 µs (Middlebrooks, 2004). The differences in time constants between intra-scalar and intra-neural stimulation might reflect soma versus fiber sites of action-potential initiation, although the many technical differences among the previous studies also could have contributed to differences. In our present preparation, we have the opportunity to make direct comparisons of temporal-integration time constants between intra-scalar and intra-neural stimulation sites using the same animals and the same inferior-colliculus recording sites. Our preliminary analysis of data from 2 cats are consistent with the hypothesis that the time constant for temporal integration is shorter for intra-neural than for intra-scalar stimulation. We intend to continue these measurements in more animals in the next quarter.

We have begun tests of interactions among simultaneously stimulated channels. In a previous study of auditory cortical responses to intra-scalar stimulation in the guinea pig, we showed that two intra-scalar electrodes stimulated as monopoles produced widely overlapping patterns of excitation (Middlebrooks, 1994). When stimulated simultaneously, thresholds were reduced, consistent with a quantitative model involving simple addition of electrical fields from the two electrodes. Those results indicated that stimulation at one electrode had a substantial impact on the operating range at the other electrode. We observed comparable channel interactions in the present preparation using intra-scalar stimulation with recording in the inferior colliculus. For instance, stimulating the most apical intra-scalar electrode at a level 4 dB below its own threshold lowered by ~10 dB the threshold of other intra-scalar electrodes located as far as 5.25 mm basal from the most apical electrode.

Intra-neural stimulation, however, produced markedly less channel interaction. When one intra-scalar electrode was stimulated at a level 3 dB below its own threshold, the threshold on another electrode 200 µm away was lowered by only 2 dB, the threshold 400 µm away was lowered by 1 dB, and there was negligible effect on more distant electrodes. In another stimulating-array placement in the same animal, distal, middle, and proximal electrode sites on the array activated ICC regions corresponding respectively to middle, apical, and basal turns of the cochlea. Simultaneous stimulation of any of those electrodes at levels as much as 4 dB above the electrode's own threshold had negligible effect on the threshold for activation of the other electrodes. The pattern of ICC activation resulting from any of those three electrodes closely resembled the sum of the patterns resulting from stimulation of each electrode separately. That is, the stimulation sites showed largely independent activation of discrete portions of the tonotopic representation. Again, these observations will be pursued in more animals in the next quarter.

3. Plans for next quarter:

- Continue studies of the cochleotopic projection from the auditory nerve to the ICC using a lateral trans-bulla approach. We hope to complete data acquisition in a few more animals so that we can prepare a publication describing the basic characteristics of intra-neural stimulation with this approach.
- Continue studies two-pulse temporal integration, interaction between simultaneously stimulated electrodes, and phase locking to the fine structure of electrical pulse trains.
- Design and build a prototype of a guide-tube/micro-positioner device that will be needed for our planned chronic recording from the ICC.

4. References

Caree, LA, van den Honert, C, Finley, CC, Miller, RL (2000): Evaluation of a model of the cochlear neural membrane. I. Physiological measurement of membrane characteristics in response to intrameatal electrical stimulation. Hearing Res. 146:143-152.

Dynes, SBC (1996): *Discharge characteristics of auditory nerve fibers for pulsatile electrical stimuli*. Doctoral Dissertation, Massachusetts Institute of Technology.

Middlebrooks, JC (2004): Effects of cochlear-implant pulse rate and inter-channel timing on channel interactions and thresholds. J.Acoust.Soc.Am. 116: 452-468.

5. Appendix:

Abstract of a poster presented at the Neural Interface Workshop.